

Amendments to the Specification

Please replace the substitute Sequence Listing (1 page) filed on June 16, 2003 with the second substitute Sequence Listing (1 page) filed herewith.

Please replace the paragraph beginning at page 4, line 19, with the following rewritten paragraph:

~~PCT/EP/04396~~ PCT/EP97/04396 (WO 98/07036) teaches a process for determining the status of an organism by peptide measurement. The reference teaches the measurement of peptides in a sample of the organism which contains both high and low molecular weight peptides and acts as an indicator of the organism's status. The reference concentrates on the measurement of low molecular weight peptides, i.e. below 30,000 Daltons, whose distribution serves as a representative cross-section of defined controls. Contrary to the methodology of the instant invention, the '396 patent strives to determine the status of a healthy organism, i.e. a "normal" and then use this as a reference to differentiate disease states. The present inventors do not attempt to develop a reference "normal", but rather strive to specify particular markers which are evidentiary of at least one specific disease state, whereby the presence of said marker serves as a positive indicator of disease. This leads to a simple method of analysis which can easily be

performed by an untrained individual, since there is a positive correlation of data. On the contrary, the '396 patent requires a complicated analysis by a highly trained individual to determine disease state versus the perception of non-disease or normal physiology.

Please replace the paragraph (first amended on June 16, 2003) beginning at page 19, line 2, with the following re-written paragraph:

FIGURE 1 is a representation of derived data which characterizes a disease specific marker having a particular sequence (~~amino acid residues 2-17 of~~ SEQ ID NO:1) useful in evidencing and categorizing at least one particular disease state. Each patient listed in the data table shows the presence of disease specific marker (~~amino acid residues 2-17 of~~ SEQ ID NO:1) in their serum.

Please replace the paragraph beginning at page 22, line 19, with the following re-written paragraph:

Chelating ~~Sepharose~~ SEPHAROSE Mini Column

1. Dilute Sera in Sample/Running buffer;
2. Add Chelating ~~Sepharose~~ SEPHAROSE slurry to column and allow column to pack;

3. Add UF water to the column to aid in packing;
4. Add Charging Buffer once water is at the level of the resin surface;
5. Add UF water to wash through non bound metal ions once charge buffer washes through;
6. Add running buffer to equilibrate column for sample loading;
7. Add diluted serum sample;
8. Add running buffer to wash unbound protein;
9. Add elution buffer and collect elution fractions for analysis;
10. Acidify each elution fraction.

Please replace the paragraph (first amended on April 19, 2002 in the Supplemental Preliminary Amendment and again in the Amendment filed on June 16, 2003) beginning at page 27, line 17 with the following re-written paragraph:

As a result of these procedures, the disease specific marker ~~consisting of amino acid residues 2-17~~ of SEQ ID NO:1 was found. This marker is characterized as a C3F fragment from the complement system having a molecular weight of about 1998 daltons. The characteristic profile of the marker is set forth in Figure 2. As easily deduced from the data set forth in Figure 1, this marker is

indicative of an individual suffering from Type II diabetes.

Please replace the paragraph beginning at page 36, line 2, with the following re-written paragraph:

The instant invention involves the use of a combination of preparatory steps in conjunction with mass spectroscopy and time-of-flight detection procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with reference to their ability to evidence at least one particular disease state; thereby enabling a diagnostician to gain the ability to characterize either the presence or absence of [[said]] at least one disease state relative to the recognition of the presence and/or the absence of [[said]] the biopolymer.